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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HORNING, MICHELLE S	
ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/675,980	IIAN ET AL.	
	Examiner	Art Unit	
	MICHELLE HORNING	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 6, 11, 43-45, 47-52, 54, 59, 60, 75, 76, 97, 109, 120, 125, 126, 151, 157, 161-169, 184, 191* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-118,120-123,125,126,129-151,154-169,171-177,183-185,187,189-191,197,198 and 200-202.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 2-5,7-10,12-42,46,53,55-58,61-74,77-96,98-108,110-118,121-123,129-150,154-156,158-160,171-177,183,185,187,189,190,197,198 and 200-202.

DETAILED ACTION

This action is responsive to communication filed 3/16/2010.

Any rejection(s) and/ or objection(s) not reiterated herein have been withdrawn.

To allow entry of the rejection(s) set forth herein, the instant office action is non-final.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 184 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 184 recites the limitation "said immune-mediated or immune-related disease or disorder" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claims 1, 6, 11, 43-45, 47-52, 54, 59, 60, 75, 76, 97, 109, 120, 125, 126, 151, 157, 161-168, 184 and 191 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention. The claims are drawn to (in part): a method for the treatment of a disease in a mammalian subject comprising administering to said subject an effective amount of a mammalian intermediary metabolite, wherein said intermediary metabolite is a lipid or glycolipid, wherein the pathogenesis of the disease is derived from an inflammatory immune response (see claim 1).

The following quotation from section 2163 of the MPEP is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see i)(A), above), reduction to drawings (see i)(B), above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i)(C), above). See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed or through disclosure of a functional characteristic of the claimed genus coupled with a known or disclosed non-functional characteristic (structure) that correlates to the function.

Structurally, the claims are broad with respect to a genus of a mammalian metabolic intermediate comprising a lipid or a glycolipid.

The instant specification also provides the following regarding what a mammalian metabolite is: The present invention provides methods for the treatment of a disease in a mammalian subject by the administration of an effective amount of an intermediary metabolite to the subject. The intermediary metabolite includes, but is not limited to a T cell receptor ligand, a lipid, a polar lipid, a conjugated biomolecule, a glycolipid, a lipoprotein, an apolipoprotein, a glycoprotein, a monosaccharide or polysaccharide ceramide, a glucosylceramide, a galactosylceramide, a glucocerebroside, a glucocerebroside analogue or derivative, a sphingosine, a sphingolipid or a ceramide. In a preferred embodiment of the invention, the mammalian subject is a human being. See para. 43.

According to the prior art, Sweeley (Pure & Appl. Chem., 1989) states that there are more than 200 compounds in the class of glycosphingolipids that have been isolated and chemically characterized (abstract). Sweeley also cites the following: "Simple arithmetic calculations indicate the enormous diversity of structures that are theoretically possible with a few different sugar constituents, disregarding the heterogeneity of the ceramide moiety. For example, there could be about 500 million different glycosphingolipids, containing a core of 5 sugar residues (Glc, Gal, GlcNAc and alNAc combinations) in the pyranose ring form and one or two Fuc or NeuAc residues" (p. 1308, para. 2). A more recent review describes the glycosphingolipids as having a huge heterogeneity of structure comprising more than 60 different sphingoid

bases and more than 300 different oligosaccharide chains that have been described at the time of the publication (Degroote et al., Sem in Cell & Dev Bio, 2004).

While both the instant specification and the prior art teach such a diversity of structures for an intermediate metabolite, note that *functionally* the claims are specific. For example, claim 6 requires that the result of the administration of an intermediary metabolite comprises changes in cytokine response, claim 44 requires the result is a decrease in the number or function of regulatory, immune-regulatory or NKT cells and claim 45 requires that the result is an increase in the number or function of regulatory, immune-regulatory or NKT cells.

The instant specification provides no structure to function correlations for the specific claimed functional limitations and merely describes the modulatory effects following the administration of a *single* compound, glucocerebroside. In view of claims 44 and 45 drawn to either a decrease or an increase of NKT cells following the administration of an intermediary metabolite, note that the specification only demonstrates an increase in NKT cells; see Figures 10-12. Based on the instant specification, it is not clear what the required structural features of an intermediary metabolite are so that administration of such would lead to a decrease in NKT cells as claimed. Thus, the instant specification fails to describe the genus of mammalian intermediary metabolites in a reasonable manner so that one of ordinary skill in the art can readily envision the claimed genus as well as establish any structure to function correlation of the genus of metabolites necessary in order to perform the specific functions as claimed.

In view of the broad scope of the claims for a mammalian intermediary metabolite as evidenced by the instant specification (para. 43) and the prior art teachings and the lack of structure to function correlations for an adequate number of species, the claims are rejected for lacking adequate written description in the instant specification.

Claims 1, 6, 11, 43-45, 47-52, 54, 59, 60, 75, 76, 97, 109, 120, 125, 126, 151, 157, 161-169, 184 and 191 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for modulating immune responses via administration of glucocerebroside, does not reasonably provide enablement for the treatment of any and all diseases in a mammalian subject comprising administering any and all mammalian intermediary metabolites. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/ use the invention commensurate in scope with these claims.

Enablement is considered in view of the *Wands* factors.

Nature of the invention. The claims are drawn to (in part): a method for the treatment of a disease in a mammalian subject comprising administering to said subject an effective amount of a mammalian intermediary metabolite, wherein said intermediary metabolite is a lipid or glycolipid, wherein the pathogenesis of the disease is derived from an inflammatory immune response (see claim 1).

Scope of the invention. The claims are extremely broad with respect to both an intermediary metabolite and a disease that is derived from an inflammatory immune

response. Also, see claim 157 which is drawn to a list of different diseases as well as "any other immune-related or immune-mediated disorder or disease".

State of the prior art. As noted above, the prior art describes the enormity of intermediary metabolites in view of structure comprising a lipid or a glycolipid; see Degroote et al., Sem in Cell & Dev Bio, 2004 and Sweeley, Pure & Appl. Chem., 1989. The prior art also describes a method of modulating an immune response in a mammalian subject comprising administering an effective amount of a specific mammalian intermediary metabolite which comprises a glycolipid, wherein the specific intermediary metabolite is either a ganglioside or a glucocerebroside (see Gizurarson, US Patent 5942237 and Belchetz et al. Lancet, 1977).

Working examples. The examples are drawn to the immunomodulatory effects of administering a *single* compound, glucocerebroside, wherein the effects include modulation of the number of NKT cells, CD4/CD8 ratio and glucose tolerance. The working examples fail to show how these immunomodulatory effects correlate to the actual treatment of any and all diseases derived from an inflammatory response or how this relates to mammalian intermediary metabolites of differential structures.

Guidance in the specification. The specification provides no guidance regarding how the administration of any and all mammalian intermediary metabolites may successfully treat any and all diseases derived from an inflammatory immune response. Further, there are no dosing regimens or time durations of treatment or structure to function correlation provided.

Predictability of the art. The ordinary artisan could not predict the correlation of an intermediary metabolite to its function in treating a broad genus of diseases. As noted above, the diseases listed in claim 157 are unrelated in origin, each of which may have distinct symptoms, etiologies, structures, nucleic acids, time course of incubation and infection, etc.

Amount of experimentation necessary. Based on the content of the instant specification, much undue experimentation would be necessary in order to determine if treatment of an entire genus of diseases derived from an inflammatory immune response via administration of an entire genus of mammalian metabolites would be successful. The ordinary artisan would be required to generate actual data to determine if such successful treatment is possible. The specification fails to provide guidance on what structural characteristics of a mammalian intermediary metabolite would be required, its required mechanism of action or its structure to function correlation to the instant claimed methods.

Given the discussion above, it would require undue experimentation for the ordinary artisan to perform the full scope of the method as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6, 11, 43-45, 47-52, 59, 60, 75, 76, 97, 109, 120, 125, 126, 151, 157 and 161-169 are rejected under 35 U.S.C. 102(b) as being anticipated by Gizurarson (US Patent No. 5942237, published August 24, 1999) as further evidenced by Ogawa (US Patent No. 5101026).

The claims are drawn to (in part): a method for the treatment of a disease in a mammalian subject comprising administering to said subject an effective amount of a mammalian intermediary metabolite, wherein said intermediary metabolites is a lipid or glycolipid, wherein the pathogenesis of the disease is derived from an inflammatory immune response.

Gizurarson describes a method of inducing an immunomodulatory response in a mammalian subject witih a respiratory disease comprising administering an effective amount of the mammalian intermediary metabolite ganglioside which comprises a glycolipid, wherein the disease is rhinovirus, influenza, tuberculosis and respiratory syncytial virus (see col. 2, lines 45+ and col. 5, lines 24+; meeting “Lung Disease” and “any other immune-related or immune mediated disorder” in instant claim 157). Note that a ganglioside comprises a glucosylceramide which is a ceramide to which glucose is attached (see col. 2, lines 46+ and pg. 3, para. 2 of the instant specification), meeting the limitations of a glycolipid, a polar lipid and a glycolid comprising a monosaccharide ceramide which comprises a glucosylceramide (see instant claims including claims 1, 11, 43-45, 59, 60, 97, 120, 125 and 169). The authors further describe administering antigens with the ganglioside via intranasal administration (col. 1, lines 62+; col. 2 and instant claims 151).

Note that claims 75, 109 and 126 only further defines what the antigen may be but does not require its administration. These claims depend on claims 11, 59 and 97 and none of the claims require the administration of the antigen. The same applies to claim 76 wherein the antigen presenting cell is further defined but it administration is not required; see its dependent claim 59.

Ogawa is cited only to demonstrate that ganglioside acts as an intermediary in proliferation of brain glandula lymphocytes and are found in human and calf brains, meeting the limitation of a “mammalian intermediary metabolite” (see col. 1, lines 41+ and col. 2, line1+). Note that the instant specification provides no definition for an intermediary metabolite and does not limit the claimed metabolite to any specific metabolism or biopathway.

It is noted that many of the instant claims, including claims 6, 43-45, 47-52, 59, 60, 97 and 161-168, comprise limitations that are not active steps in the claims, but are only the mechanisms of action which occur following the single active step of administration of a mammalian intermediary metabolite, for example, "the result of said administration comprises changes in cytokine responses“(see claim 6). The prior art discloses the same active step of administrating of an intermediary metabolite found in the instant claims. Thus, the same mechanisms of action must occur because the composition/method use and its properties are inseparable.

Also see MPEP 2112 [R-3] stating that something which is old does not become patentable upon the discovery of a new property. In this case, the method of administering an intermediary metabolite or a known composition is a known method as

taught by the prior art. The authors describe observations different than those claimed; however, the claiming of a new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable.

Claims 1, 6, 11, 43-45, 47-52, 59, 60, 75, 76, 97, 109, 120, 125, 126, 151, 157 and 161-169 are rejected under 35 U.S.C. 102(b) as being anticipated by Belchetz (The Lancet, 1977).

The claims are drawn to (in part): a method for the treatment of a disease in a mammalian subject comprising administering to said subject an effective amount of a mammalian intermediary metabolite, wherein said intermediary metabolites is a lipid or glycolipid, wherein the pathogenesis of the disease is derived from an inflammatory immune response.

Belchetz et al. describes the intravenous administration of glucocerebroside in a patient with Gaucher's disease and observed the differential immune responses, including changes in plasma levels of enzymes and liver size (see whole document including METHODS on p. 116, col. 1, para. 3-4). Note that this disease meets a "metabolic syndrome" and "any other immune-related or immune mediated disorder" and intravenous administration is also met; see claims 151 and 157. Glucocerebroside meets the limitation of a mammalian intermediary metabolite, given the authors describe that this metabolite was obtained from human placentas (p. 116, col. 1, para. 4). A glucocerebroside also meets the structural limitations of polar lipid and a glycolipid comprising a monosaccharide ceramide which comprises a glucosylceramide (see claims 120, 125 and 169).

Note that claims 75, 109 and 126 only further defines what the antigen may be but does not require its administration. These claims depend on claims 11, 59 and 97 and none of the claims require the administration of the antigen. The same applies to claim 76 wherein the antigen presenting cell is further defined but it administration is not required; see its dependent claim 59.

It is noted that many of the instant claims, including claims 6, 43-45, 47-52, 59, 60, 97 and 161-168, comprise limitations that are not active steps in the claims, but are only the mechanisms of action which occur following the single active step of administration of a mammalian intermediary metabolite, for example, "the result of said administration comprises changes in cytokine responses"(see claim 6). The prior art discloses the same active step of administrating of an intermediary metabolite found in the instant claims. Thus, the same mechanisms of action must occur because the composition/method use and its properties are inseparable.

Also see MPEP 2112 [R-3] stating that something which is old does not become patentable upon the discovery of a new property. In this case, the method of administering an intermediary metabolite or a known composition is a known method as taught by the prior art. The authors describe observations different than those claimed; however, the claiming of a new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6, 11, 43-45, 47-52, 59, 60, 76, 97, 120, 125, 151, 157, 161-169 and 184 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Marinier (US Patent 5747463) and Gizurarson (US Patent No. 5942237) and/ or Belchetz (The Lancet, 1977) and as further evidenced by Ogawa (US Patent No. 5101026).

The claims are further drawn to the treatment of colitis (claim 184).

Marinier discloses the administration of an effective amount of a modified intermediary metabolite comprising a glycolipid to a subject with colitis, wherein the pathogenesis of the disease is derived from an inflammatory immune response (i.e. elected species, colitis); see abstract, Formula I and col. 2, lines 47+. Note that Formula I depicts the structure of an intermediary metabolite as possessing a glycolipid, monosaccharide ceramide and galactosylceramide and a therapeutically effective

amount is described (col. 3, lines 37+). The authors describe a step of administration including oral, intravenous, intramuscular etc. (see col. 33, lines 35+ and instant claim 151).

Marinier does not disclose using a "mammalian" intermediate metabolite.

Gizurarson teaches the administration of the mammalian intermediate metabolite, ganglioside (see whole document). Note that a ganglioside comprises a glucosylceramide which is a ceramide to which glucose is attached (see col. 2, lines 46+ and pg. 3, para. 2 of the instant specification), meeting the limitations of a glycolipid, a polar lipid and a glycolid comprising a monosaccharide ceramide which comprises a glucosylceramide.

Belchetz et al. describes the intravenous administration of glucocerebroside in a patient and observed the differential immune responses, including changes in plasma levels of enzymes and liver size (see whole document including METHODS on p. 116, col. 1, para. 3-4). Glucocerebroside meets the limitation of a mammalian intermediary metabolite, given the authors describe that this metabolite was obtained from human placentas (p. 116, col. 1, para. 4). A glucocerebroside also meets the structural limitations of polar lipid and a glycolipid comprising a monosaccharide ceramide which comprises a glucosylceramide (see claims 120, 125 and 169).

It would have been obvious for one of ordinary skill in the art to incorporate a known mammalian intermediary metabolite, including a ganglioside or glucocerebroside, in the method taught by Marinier. One would have been motivated to use a ganglioside or a glucocerbroside as an equivalent compound. Further noted is

that the intermediary metabolites described by Gizurarson and Belchetz share common structural features (e.g. glycolipid, ceramides etc.). There would have been a reasonable expectation of success given the administration of intermediary metabolites is a known method as evidenced by the prior art. The invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Ogawa is cited only to demonstrate that ganglioside acts as an intermediary in proliferation of brain glandula lymphocytes and are found in human and calf brains, meeting the limitation of a “mammalian intermediary metabolite” (see col. 1, lines 41+ and col. 2, line1+). Note that the instant specification provides no definition for an intermediary metabolite and does not limit the claimed metabolite to any specific metabolism or biopathway.

It is noted that many of the instant claims, including claims 6, 43-45, 47-52, 59, 60, 97 and 161-168, comprise limitations that are not active steps in the claims, but are only the mechanisms of action which occur following the single active step of administration of a mammalian intermediary metabolite, for example, "the result of said administration comprises changes in cytokine responses“(see claim 6). The prior art discloses the same active step of administrating of an intermediary metabolite found in the instant claims. Thus, the same mechanisms of action must occur because the composition/method use and its properties are inseparable.

Also see MPEP 2112 [R-3] stating that something which is old does not become patentable upon the discovery of a new property. In this case, the method of administering an intermediary metabolite or a known composition is a known method as

taught by the prior art. The authors describe observations different than those claimed; however, the claiming of a new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable.

Claims 75, 109 and 126 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Marinier (US Patent 5747463) and Gizurarson (US Patent No. 5942237) and/ or Belchetz (The Lancet, 1977) as applied to claims 1, 6, 11, 43-45, 47-52, 59, 60, 97, 120, 125, 151, 157, 161-169 and 184 above, and further in view of Das (US Patent 5869048) and as further evidenced by Ogawa (US Patent No. 5101026).

The claims are further drawn to administering allogenic antigens obtained from donors suffering from an immune-related or immune-mediated disorder or disease.

The combination of Marinier, Gizurarson and/ or Belchetz (as evidenced by Ogawa) provides a method of administering a mammalian intermediary metabolite to a subject with colitis. Note that Gizurarson further teaches administering antigens with the ganglioside via intranasal administration (col. 1, lines 62+; col. 2 and instant claims 151).

The combined teachings do not disclose administering an antigen obtained from donors suffering from an immune-related or immune-mediated disorder or disease.

Das describes a method of vaccinating a human against ulcerative colitis which comprises administering a therapeutically effective amount of a colonic antigen associated with ulcerative colitis obtained from a human (see Abstract and col. 3, lines 16+).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to further administer a colonic antigen in the method taught by Marinier, Gizurarson and/ or Belchetz (as evidenced by Ogawa). One of ordinary skill in the art at the time the invention was made would have been motivated to do so for the advantage of vaccinating a subject against ulcerative colitis as taught by Das. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success given the underlying techniques are widely known and commonly used in the prior art. The invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Ogawa is cited only to demonstrate that ganglioside acts as an intermediary in proliferation of brain glandula lymphocytes and are found in human and calf brains, meeting the limitation of a “mammalian intermediary metabolite” (see col. 1, lines 41+ and col. 2, line1+). Note that the instant specification provides no definition for an intermediary metabolite and does not limit the claimed metabolite to any specific metabolism or biopathway.

It is noted that many of the instant claims, including claims 6, 43-45, 47-52, 54, 59, 60, 97 and 161-168, comprise limitations that are not active steps in the claims, but are only the mechanisms of action which occur following the single active step of administration of a mammalian intermediary metabolite, for example, "the result of said administration comprises changes in cytokine responses“(see claim 6). The prior art discloses the same active step of administrating of an intermediary metabolite found in

the instant claims. Thus, the same mechanisms of action must occur because the composition/method use and its properties are inseparable.

Also see MPEP 2112 [R-3] stating that something which is old does not become patentable upon the discovery of a new property. In this case, the method of administering an intermediary metabolite or a known composition is a known method as taught by the prior art. The authors describe observations different than those claimed; however, the claiming of a new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable.

Claims 54, 76 and 191 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Marinier (US Patent 5747463) and Gizurarson (US Patent No. 5942237) and/ or Belchetz (The Lancet, 1977) as applied to claims 1, 6, 11, 43-45, 47-52, 59, 60, 97, 120, 125, 151, 157, 161-169 and 184 above, and further in view of Collins (PGPUB 20020141977) and Liotta (US Patent 6610835) and as further evidenced by Ogawa (US Patent No. 5101026).

The claims are further drawn to administering antigen presenting cells, including dendritic cells (claims 54 and 76) and using a subject that has been without food for a minimum of 12 hours prior to administration.

The combination of Marinier, Gizurarson and/ or Belchetz (as evidenced by Ogawa) provides a method of administering a mammalian intermediary metabolite to a subject with colitis.

The combined teachings do not disclose administering antigen presenting cells, including dendritic cells (claims 54 and 76) and administering to a subject that has been without food for a minimum of 12 hours prior to administration.

Collins describes a general method of immunotherapy based on antigen presenting cells including dendritic cells for the prevention and/or treatment of various diseases such as inflammatory diseases (see Title and Abstract).

Liotta discloses that sphinogolipids are found in a number of foods, including wheat flour, potato and beans (col. 9, lines 24+).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to further administer a dendritic cell to a food deprived animal using the method taught by the combination of Marinier, Gizurarson and/ or Belchetz (as evidenced by Ogawa).

One of ordinary skill in the art at the time the invention was made would have been motivated to use dendritic cells for the advantage of providing a known method of immunotherapy to subject as taught by Collins.

One of ordinary skill in the art at the time the invention was made would have been motivated to use animals that are food deprived in order to better control the amount of intermediary metabolites in a subject and to regulate intermediary metabolite-induced effects. Note that one of ordinary skill in the art at the time the invention was made would have been motivated to alter the duration (hours) of food deprivation in order to optimize the effects of the administered metabolites.

One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success given the underlying techniques are widely known and commonly used in the prior art. The invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 6, 11, 43-45, 47-52, 59, 60, 97, 120, 125, 151, 157 and 161-169 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 4-6 of copending Application No. 10/375, 906 (PGPUB 20040177522) in view of Stephenson and Zambon (*Occup. Med*, 2002). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a method of the same step of

administering the same compound, an intermediary metabolite. Note that the claims of the '906 application are drawn to subjects with viral infections. This is within the scope of the pulmonary, respiratory diseases of the claimed invention because such diseases include viral influenza (see abstract of Stephenson and Zambon).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 6, 11, 43-45, 47-52, 59, 60, 97, 120, 125, 151, 157 and 161-169 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 12, 15-17 and 22-24 of copending Application No. 10/733,488 (PGPUB 20040171526) in view of Stephenson and Zambon (*Occup. Med*, 2002) and Hansen-Flaschen (*Ann Intern Med*, 2003). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a method of the same step of administering the same compound, an intermediary metabolite. Note that the claims of the '488 application are drawn to subjects with cancer, bacterial and viral infections. This is within the scope of the pulmonary, respiratory diseases of the claimed invention because such diseases include viral influenza (see abstract of Stephenson and Zambon), lung cancers and bacterial tuberculosis (see p. 322, col. 2 and p. 321, col. 1, respectively of Hansen-Flaschen).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 6, 11, 43-45, 47-52, 59, 60, 97, 120, 125, 151, 157 and 161-169 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 50-52, 55, 57, 59 and 62 of copending Application No. 10/733, 489 (PGPUB 20040171527) in view of Stephenson and Zambon (*Occup. Med*, 2002) and Hansen-Flaschen (*Ann Intern Med*, 2003). Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a method of the same step of administering the same compound, an intermediary metabolite. Note that the claims of the '489 application are drawn to subjects with cancer and viral infections. This is within the scope of the pulmonary, respiratory diseases of the claimed invention because such diseases include viral influenza (see abstract of Stephenson and Zambon) and lung cancers (see p. 322, col. 2 of Hansen-Flaschen).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 6, 11, 43-45, 47-52, 59, 60, 97, 120, 125, 151, 157 and 161-169 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 9-11, 21-25, 27-31, 36-38, 48 and 49 of copending Application No. 11/287,502 . Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a method of the same step of administering the same compound, an intermediary metabolite.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 6, 11, 43-45, 47-52, 59, 60, 97, 120, 125, 151, 157 and 161-169 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2 and 5 of copending Application No. 12/746, 430. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a method of the same step of administering the same compound, an intermediary metabolite.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's arguments with respect to claims 1, 6, 11, 43-45, 47-52, 54, 59, 60, 75, 76, 97, 109, 120, 125, 126, 151, 157, 161-169, 184 and 191 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELLE HORNING whose telephone number is (571)272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ZACHARIAH LUCAS can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/M. H./
Examiner, Art Unit 1648

/Zachariah Lucas/
Primary Examiner, Art Unit 1648